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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/508,907	05/24/2000	RAINER HOFFMANN		3754

7590 02/06/2004

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EXAMINER	
GHALI, ISIS A D	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 02/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/508,907	HOFFMANN ET AL.	
	Examiner	Art Unit	
	Isis Ghali	1615	

-- The MAILING DATE of this communication app ars on the cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,30 and 116* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14, 16-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The receipt is acknowledged of applicant's amendment, filed 11/17/2003.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/17/2003 has been entered.

Specification

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC (See 37 CFR 1.52(e)(5) and MPEP 608.05. Computer

program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text are permitted to be submitted on compact discs.) or
REFERENCE TO A "MICROFICHE APPENDIX" (See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.)

(e) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.

(f) BRIEF SUMMARY OF THE INVENTION.

(g) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).

(h) DETAILED DESCRIPTION OF THE INVENTION.

(i) CLAIM OR CLAIMS (commencing on a separate sheet).

(j) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).

(k) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

2. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-14, 16-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the morphine, does not reasonably provide enablement for all morphine alkaloids such as: codeine, heroin, ethylmorphine,

levorphanol, or hydromorphone. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: the nature of the invention; the breadth of the claims; the state of the prior art; the relative skill of those in the art; the amount of direction or guidance presented; the predictability or unpredictability of the art; the presence or absence of working examples; and the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The nature of the invention:

The invention provides transdermal or transmucosal composition for administering at least one morphine alkaloid, the composition consisting essentially of at least one morphine alkaloid as an addition salt with an organic acid, and olive oil. The entire specification disclosed morphine, and not the whole class of morphine alkaloids. Support for species is not a support for genus.

The breadth of the claims: The claims are very broad. The claims encompass a wide class of morphine alkaloids including codeine, heroin, ethylmorphine, levorphanol, and hydromorphone, each in combination with olive oil to provide enhanced flux.

The state of the prior art:

The morphine alkaloids of the invention include codeine, heroin, ethylmorphine, levorphanol, or hydromorphone with olive oil. However, the art does not teach these species of morphine alkaloids with olive oil. The art recognized the morphine alkaloids with other permeation enhancer.

The relative skill of those in the art:

The relative skill of those in the art is high.

The amount of direction or guidance presented:

The specification provides no guidance, in the way written description, on each species of morphine alkaloids including codeine, heroin, ethylmorphine, levorphanol, or hydromorphone as acid addition salt with organic acid transdermally or transmucosally with olive oil and the flux of each of the claimed species. The specification disclosed only morphine. It is not obvious from the disclosure of morphine if the other morphine alkaloids will work with olive oil and provide the same flux. In re *Dreshfield,* 110 F.2d 235, 45 USPQ 36 (CCPA 1940), gives this general rule: "It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result." The article "Broader than the Disclosure in Chemical Cases," 31 J.P.O.S. 5, by Samuel S. Levin covers this subject in detail. A disclosure should contain representative examples which provide reasonable assurance to one skilled in the art that the compounds fall within the scope of a claim will possess the alleged activity.

See *In re Riat et al.* (CCPA 1964) 327 F2d 685, 140 USPQ 471; In re Barr et al. (CCPA 1971) 444 F 2d 349, 151 USPQ 724.

The predictability or unpredictability of the art:

The lack of guidance from the specification and from the prior art with regard of a transdermal or transmucosal composition for administering at least one morphine alkaloid, the composition consisting essentially of at least one morphine alkaloid as an addition salt with an organic acid and olive oil makes practicing the claimed invention unpredictable in the terms of the flux of other species of morphine alkaloids.

The presence or absence of working examples:

The specification discloses only morphine in all the examples. No working examples to show the use of other species of morphine alkaloids. Therefore, the specification has enabled only the species "morphine".

The quantity of experimentation necessary:

Since the behavior of other species of morphine alkaloids, other than morphine, is unpredictable, and when the above factors are weighed together, one of ordinary skill in the art would be burdened with undue experimentation to determine the flux of all the species of the morphine alkaloids with olive oil.

5. Claims 1-14, and 16-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application

was filed, had possession of the claimed invention. The specification provides no support for transdermal or transmucosal composition for administering at least one morphine alkaloid of formula I, the composition consisting essentially of at least one morphine alkaloid as an addition salt with an organic acid, wherein the acid salt of morphine alkaloid having a property of penetrating the skin as defined by a flux of 2.34 $ug/cm^2.h$ for a suspension of the acid salt consisting essentially of the acid salt and olive oil. The support in the specification in figure 4, under example 6, is for one morphine salt, namely is for examples 2, 3, 4, 5, 6, 7, 9 and 10, which meet the claim criteria of flux of at least 2.34 $ug/cm^2.h$. No support for the claimed genus having this flux of at least 2.34 $ug/cm^2.h$ with the olive oil. Support for a species is not a support for genus.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-14, 16-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims lack clarity as they recite the organic acid is selected from monoesters. Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "monoesters

of dicarboxylic acids with monhydric alcohols" and the term "carboxypropyl or carboxybutyl" in claims 1 and 13 are defining esters, while they are used by the claim to mean "organic acids that from acid addition salts with the morphine alkaloids.

8. Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "bond C_7/C_8 is saturated" in claims 18 and 27 is used by the claim to mean "no double bond between C_7/C_8", while the formula shows unsaturated bond between C_7/C_8.

9. Claims 18 and 27 recite the limitation "saturated bond at C_7/C_8 " in the second line of each of the claims. There is insufficient antecedent basis for this limitation in the claims 1 and 13 because the formula shows unsaturated bond at C_7/C_8.

10. The claims are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors. The examiner suggests deleting the words "residues", "monad residues", "dyad residues" from claims 1 and 13. The examiner suggests to rephrase the paragraph: "substituted benzoic

acids, selected from the group consisting of halogen, p- and m-hydroxy, alkyl, hydroxyalkyl, alkoxyalkyl, alkoxy-substituted benzoic acids, amino substituted benzoic acids, amino substituted benzoic acids alkylated at the N atom," to read as follows: "substituted benzoic acids, wherein the constituent is selected from the group consisting of halogen, p- and m-hydroxy, alkyl, hydroxyalkyl, alkoxyalkyl, alkoxy, amino N-alkyl amino,".

11. Regarding claim 12, the claim further adds solution of glycerin, ethylene glycol, etc. Claim 12 depends on claim 1 that has a closed language: "consisting essentially of", and the dependent claims should not further add to the composition of the generic claim.

12. Claim 16 would read better if amended to:

" The composition according to claim 1, wherein the composition in the form of a lotion, ointment, cream, gel, spray, iontophoretic device, transmucosal therapeutic system or transdermal therapeutic system that comprises a reservoir layer and a backing layer which is permeable or impermeable with respect to the active substance. "

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday through Thursday from 7:00 AM to 5:30 PM, Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page, can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Isis Ghali
Examiner
Art Unit 1615

Isis Ghali

ISIS GHALI
PATENT EXAMINER